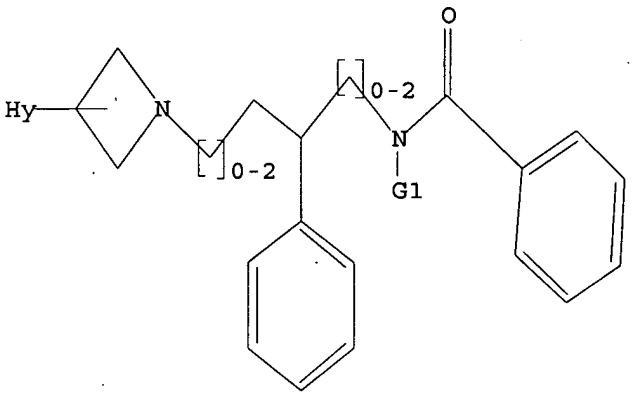
L1 STRUCTURE UPLOADED

=> d l1
L1 HAS NO ANSWERS
L1 STR



G1 Cb,Ak

Structure attributes must be viewed using STN Express query preparation.

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SAMPLE SCREEN SEARCH COMPLETED - 78 TO ITERATE

100.0% PROCESSED 78 ITERATIONS 8 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 1031 TO 2089
PROJECTED ANSWERS: 8 TO 329

L2 8 SEA SSS SAM L1

=> s l1 sss full
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FULL SCREEN SEARCH COMPLETED - 1309 TO ITERATE

100.0% PROCESSED 1309 ITERATIONS 75 ANSWERS
SEARCH TIME: 00.00.01

L3 75 SEA SSS FUL L1

=> file caplus
COST IN U.S. DOLLARS SINCE FILE ENTRY TOTAL SESSION
FULL ESTIMATED COST 172.10 172.31

FILE 'CAPLUS' ENTERED AT 10:47:31 ON 14 DEC 2007

FILE COVERS 1907 - 14 Dec 2007 VOL 147 ISS 26
FILE LAST UPDATED: 13 Dec 2007 (20071213/ED)

Effective October 17, 2005, revised CAS Information Use Policies apply. They are available for your review at:

http://www.cas.org/infopolicy.html

=> s l3
L4 11 L3

=> d ibib abs hitstr tot

L4 ANSWER 1 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2007:1333355 CAPLUS
DOCUMENT NUMBER: 147:541903
TITLE: Preparation of azetidinyl compounds as neurokinin antagonists for treating gastrointestinal disorder
INVENTOR(S): Johansson, Anders
PATENT ASSIGNEE(S): Swed.
SOURCE: U.S. Pat. Appl. Publ., 13pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2007270400	A1	20071122	US 2007-749984	20070517
PRIORITY APPLN. INFO.:			US 2006-801576P P	20060518

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

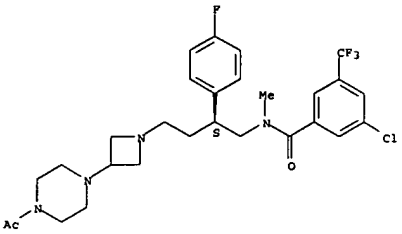
AB The present invention relates to new compds. of formula I (wherein Het is, for example, substituted piperazine), to pharmaceutical compns. comprising said compds., and to the use of said compds. in therapy. I are neurokinin antagonists with well-balanced pharmacokinetic and pharmacodynamic properties useful for treating functional gastrointestinal disorder, IBS and functional dyspepsia. The present invention further relates to processes for the preparation of compds. of formula I. For example, II was prepared by reacting 3-Chloro-N-[(2S)-2-(4-fluorophenyl)-4-oxobutyl]-N-methyl-5-(trifluoromethyl)benzamide and 1-acetyl-4-azetidin-3-ylpiperazine hydrochloride. In in vitro testing II had pKB values of 7.2-8 for human NK1, NK2, and NK3 receptors.

IT 957127-68-3P, 3-Chloro-N-[(2S)-2-(4-fluorophenyl)-4-[3-(4-acetylpiperazin-1-yl)azetidin-1-yl]butyl]-N-methyl-5-(trifluoromethyl)benzamide 957127-70-7P, 3-Chloro-N-[(2S)-2-(4-fluorophenyl)-4-[3-(4-isobutyrylpiperazin-1-yl)azetidin-1-yl]butyl]-N-methyl-5-(trifluoromethyl)benzamide
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); PKT (Pharmacokinetics); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of azetidinylpiperidine compds. as metabolically stable neurokinin antagonists for treating gastrointestinal disorders)

RN 957127-68-3 CAPLUS
CN Benzamide, N-[(2S)-4-[3-(4-acetyl-1-piperazinyl)-1-azetidinyl]-2-(4-

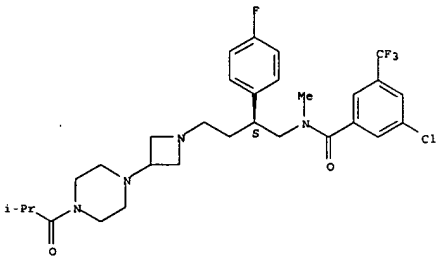
L4 ANSWER 1 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
fluorophenyl)butyl]-3-chloro-N-methyl-5-(trifluoromethyl)- (CA INDEX NAME)

Absolute stereochemistry.



RN 957127-70-7 CAPLUS
CN Benzamide, 3-chloro-N-[(2S)-2-(4-fluorophenyl)-4-[3-[4-(2-methyl-1-oxopropyl)-1-piperazinyl]-1-azetidinyl]butyl]-N-methyl-5-(trifluoromethyl)- (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 2 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2007:1333249 CAPLUS
DOCUMENT NUMBER: 147:541905
TITLE: Preparation of morpholinylazetidines as neurokinin receptor antagonists for treating gastrointestinal disorders
INVENTOR(S): Fredenwall, Marlene; Johansson, Anders
PATENT ASSIGNEE(S): Swed.
SOURCE: U.S. Pat. Appl. Publ., 10pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2007270399	A1	20071122	US 2007-749951	20070517
WO 2007136326	A2	20071129	WO 2007-SE484	20070516
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
PRIORITY APPLN. INFO.:			US 2006-801578P P	20060518

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

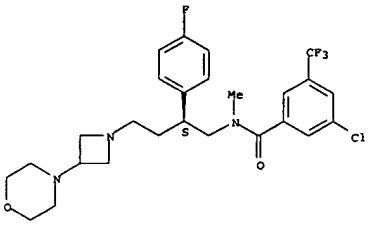
AB The present invention relates to new compds. of formula I (wherein R1 is C1-C4 alkyl, optionally substituted by ≥ 1 fluoro atoms), to pharmaceutical compns. comprising said compds., and to the use of said compds. in therapy. I are neurokinin antagonists with well-balanced pharmacokinetic and pharmacodynamic properties useful for treating gastrointestinal disorders including IBS and functional dyspepsia. The present invention further relates to processes for the preparation of compds. of formula I. For example, II was prepared by reacting 3-chloro-N-[(2S)-2-(4-fluorophenyl)-4-oxobutyl]-N-methyl-5-(trifluoromethyl)benzamide and 4-azetidin-3-ylmorpholine hydrochloride. In in vitro testing II had pKB values of 6.9-7.6 for human NK1, NK2, and NK3 receptors.

IT 957111-63-6P, 3-Chloro-N-[(2S)-2-(4-fluorophenyl)-4-[3-(morpholin-4-yl)azetidin-1-yl]butyl]-N-methyl-5-(trifluoromethyl)benzamide 957111-72-7P, 3-Chloro-N-[-2-(4-fluorophenyl)-4-[3-(morpholin-4-yl)azetidin-1-yl]butyl]-N-ethyl-5-(trifluoromethyl)benzamide 957111-73-8P, (S)-3-Chloro-N-[-2-(4-fluorophenyl)-4-[3-(morpholin-4-yl)azetidin-1-yl]butyl]-N-ethyl-5-(trifluoromethyl)benzamide 957111-74-9P, 3-Chloro-N-[-2-(4-fluorophenyl)-4-[3-(morpholin-4-

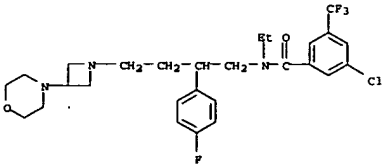
L4 ANSWER 2 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
yl)azetidin-1-yl]butyl]-N-methyl-5-(trifluoromethyl)benzamide
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); PKT (Pharmacokinetics); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; prepn. of morpholinylazetidines as neurokinin receptor antagonists for treating gastrointestinal disorders)

RN 957111-63-6 CAPLUS
CN Benzamide, 3-chloro-N-[(2S)-2-(4-fluorophenyl)-4-[3-(4-morpholinyl)-1-azetidinyl]butyl]-N-methyl-5-(trifluoromethyl)- (CA INDEX NAME)

Absolute stereochemistry.



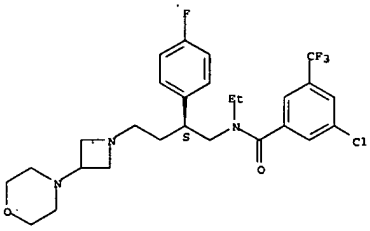
RN 957111-72-7 CAPLUS
CN Benzamide, 3-chloro-N-ethyl-N-[2-(4-fluorophenyl)-4-[3-(4-morpholinyl)-1-azetidinyl]butyl]-5-(trifluoromethyl)- (CA INDEX NAME)



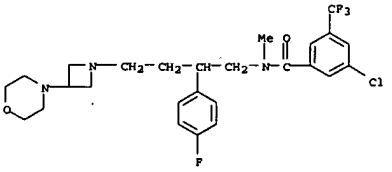
RN 957111-73-8 CAPLUS
CN Benzamide, 3-chloro-N-ethyl-N-[(2S)-2-(4-fluorophenyl)-4-[3-(4-morpholinyl)-1-azetidinyl]butyl]-5-(trifluoromethyl)- (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 2 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 957111-74-9 CAPLUS
CN Benzamide, 3-chloro-N-[2-(4-fluorophenyl)-4-[3-(4-morpholinyl)-1-azetidinyl]butyl]-N-methyl-5-(trifluoromethyl)- (CA INDEX NAME)



L4 ANSWER 3 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2007:1333221 CAPLUS
DOCUMENT NUMBER: 147:541739
TITLE: Preparation of azetidinylpiperidine compounds as neurokinin antagonists for treating gastrointestinal disorders
INVENTOR(S): Johansson, Anders; Johansson, Johan; Sigfridsson, Carl-Gustav
PATENT ASSIGNEE(S): Swed.
SOURCE: U.S. Pat. Appl. Publ., 16pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2007270398	A1	20071122	US 2007-747322	20070511
PRIORITY APPLN. INFO.:			US 2006-801577P P	20060518

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

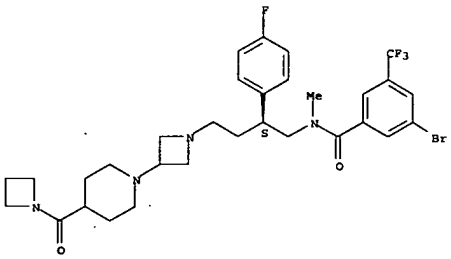
AB The present invention relates to new compds. of formula I (wherein R1 and R2 are independently H, Me, and Et, or R1 and R2 form a 4-6-membered ring together with the amide nitrogen, said ring optionally containing an oxygen atom; and X is Br or Cl), to pharmaceutical compns. comprising said compds., and to the use of said compds. in therapy. I are neurokinin antagonists with well-balanced pharmacokinetic and pharmacodynamic properties useful for treating functional gastrointestinal disorder, IBS and functional dyspepsia. The present invention further relates to processes for the preparation of compds. of formula I. For example, II was prepared by reacting 3-bromo-N-[(2S)-2-(4-fluorophenyl)-4-oxobutyl]-N-methyl-5-(trifluoromethyl)benzamide and 1-azetidin-3-yl-4-(azetidin-1-ylcarbonyl)piperidine. In in vitro testing II had pKB values of 7-9 for human NK1, NK2, and NK3 receptors.

IT 957054-68-1P, N-[(2S)-4-[3-[4-[(Azetidin-1-yl)carbonyl]piperidin-1-yl]azetidin-1-yl]-2-(4-fluorophenyl)butyl]-3-bromo-N-methyl-5-(trifluoromethyl)benzamide 957054-70-5P, 1-[1-[(3S)-4-[[3-Bromo-5-(trifluoromethyl)benzoyl](methyl)amino]-3-(4-fluorophenyl)butyl]azetidin-3-yl]-N,N-dimethylpiperidine-4-carboxamide 957054-71-6P, 1-[1-[(3S)-4-[[3-Bromo-5-(trifluoromethyl)benzoyl](methyl)amino]-3-(4-fluorophenyl)butyl]azetidin-3-yl]-N,N-dimethylpiperidine-4-carboxamide diformate 957054-73-8P, 1-[1-[(3S)-4-[[3-Bromo-5-(trifluoromethyl)benzoyl](methyl)amino]-3-(4-fluorophenyl)butyl]azetidin-3-yl]piperidine-4-carboxamide 957054-76-1P, 3-Bromo-N-[(2S)-2-(4-

L4 ANSWER 3 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

fluorophenyl)-4-[3-[4-[(morpholin-4-yl)carbonyl]piperidin-1-yl]azetidin-1-yl]butyl]-N-methyl-5-(trifluoromethyl)benzamide
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); PKT (Pharmacokinetics); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; prepn. of azetidinylpiperidine compds. as neurokinin antagonists for treating gastrointestinal disorders)
RN 957054-68-1 CAPLUS
CN INDEX NAME NOT YET ASSIGNED

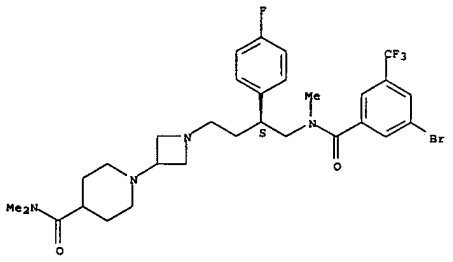
Absolute stereochemistry.



RN 957054-70-5 CAPLUS
CN 4-Piperidinecarboxamide, 1-[1-[(3S)-4-[[3-bromo-5-(trifluoromethyl)benzoyl]methylamino]-3-(4-fluorophenyl)butyl]-3-azetidinyl]-N,N-dimethyl- (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 3 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

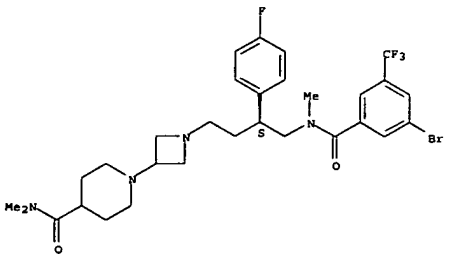


RN 957054-71-6 CAPLUS
CN Formic acid, compd. with 1-[1-[(3S)-4-[[3-bromo-5-(trifluoromethyl)benzoyl]methylamino]-3-(4-fluorophenyl)butyl]-3-azetidinyl]-N,N-dimethyl-4-piperidinecarboxamide (2:1) (CA INDEX NAME)

CM 1

CRN 957054-70-5
CMF C30 H37 Br F4 N4 O2

Absolute stereochemistry.



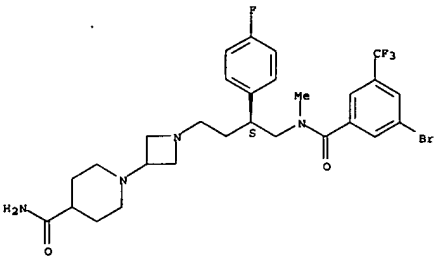
CM 2

CRN 64-18-6
CMF C H2 O2

L4 ANSWER 3 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

RN 957054-73-8 CAPLUS
CN 4-Piperidinecarboxamide, 1-[1-[(3S)-4-[[3-bromo-5-(trifluoromethyl)benzoyl]methylamino]-3-(4-fluorophenyl)butyl]-3-azetidinyl]- (CA INDEX NAME)

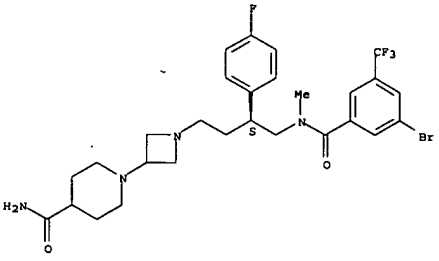
Absolute stereochemistry.



RN 957054-76-1 CAPLUS
CN Benzamide, 3-bromo-N-[(2S)-2-(4-fluorophenyl)-4-[3-[4-(4-morpholinylcarbonyl)-1-piperidinyl]-1-azetidinyl]butyl]-N-methyl-5-(trifluoromethyl)- (CA INDEX NAME)

Absolute stereochemistry.

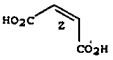
L4 ANSWER 3 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



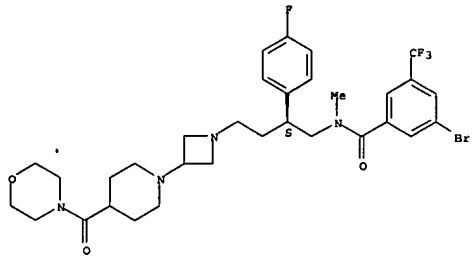
CM 2

CRN 110-16-7
CMF C4 H4 O4

Double bond geometry as shown.



L4 ANSWER 3 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



IT 957054-75-0P
RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of azetidinylpiperidine compds. as neurokinin
antagonists for treating gastrointestinal disorders)
RN 957054-75-0 CAPLUS
CN INDEX NAME NOT YET ASSIGNED

CM 1

CRN 957054-73-8
CMF C28 H33 Br F4 N4 O2

Absolute stereochemistry.

L4 ANSWER 4 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2007:438599 CAPLUS
DOCUMENT NUMBER: 146:408217
TITLE: Novel crystalline form of 3,5-dibromo-n-[(2s)-2-(-4-fluorophenyl)-4-(3-morpholin-4-ylaztidin-1-yl)butyl]-n methylbenzamide, modification B
INVENTOR(S): Ahlqvist, Matti
PATENT ASSIGNEE(S): AstraZeneca AB, Swed.
SOURCE: PCT Int. Appl., 17pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007043938	A1	20070419	WO 2006-SE1127	20061004

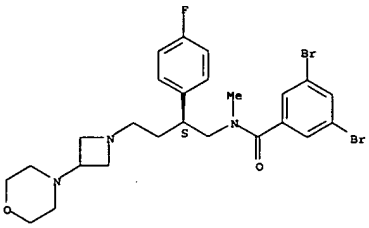
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: SE 2005-2222 A 20051007

AB The present invention relates to a novel crystalline form of 3,5-dibromo-N-[(2S)-2-(4-fluorophenyl)-4-(3-morpholin-4-ylazetidin-1-yl)butyl]-N-methylbenzamide(I). Further, the present invention also relates to the use of the novel crystalline form for the treatment of gastrointestinal disorders, pharmaceutical compns. containing it as well as
processes for the preparation of the novel crystalline form. I was slurried in 5 mL
acetonitrile and the resulting solid material was then isolated by filtration and washed with acetonitrile. The solid was shown by X-ray powder diffraction to be a mixture of two or more crystal modifications. Modification B of I was crystallized by slurring the solid from the previous
step in Et acetate in room temperature overnight. The solid material was then
isolated by evaporation of the solvent under a purge of nitrogen which was
showed to be pure modification B I. Modification B melted with a m.p. onset of 117° and may be identified by the X-ray powder diffraction.
IT 810679-97-1
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES
(Uses)
(novel crystalline form of morpholin methylbenzamide derivative)
RN 810679-97-1 CAPLUS
CN Benzamide, 3,5-dibromo-N-[(2S)-2-(4-fluorophenyl)-4-[3-(4-morpholinyl)-1-

L4 ANSWER 4 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
azetidinyl]butyl]-N-methyl- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

L4 ANSWER 5 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2007:433836 CAPLUS
DOCUMENT NUMBER: 146:408215
TITLE: Novel crystalline form of 3,5-dibromo-n-[(2s)-2-(-4-fluorophenyl)-4-(3-morpholin-4-ylazetidin-1-yl)butyl]-n-methylbenzamide, modification A
INVENTOR(S): Fredenwall, Marlene
PATENT ASSIGNEE(S): AstraZeneca AB, Swed.
SOURCE: PCT Int. Appl., 17pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007043939	A1	20070419	WO 2006-SE1128	20061004

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: SE 2005-2221 A 20051007

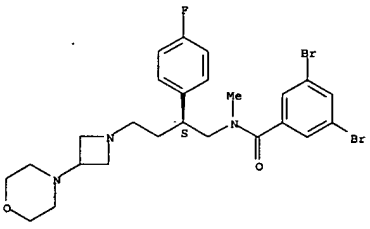
AB The present invention relates to a novel crystalline form of 3,5-dibromo-N-[(2S)-2-(4-fluorophenyl)-4-(3-morpholin-4-ylazetidin-1-yl)butyl]-N-methylbenzamide(I). Further, the present invention also relates to the use of the novel crystalline form for the treatment of gastrointestinal disorders, pharmaceutical compns. containing it as well as processes for the preparation of the novel crystalline form. I was slurried in 5 mL acetonitrile and the resulting solid material was then isolated by filtration, washed with acetonitrile, and dried. The solid was shown to be pure modification A of I. Modification A melted with a m.p. onset of 108° and may be identified by the X-ray powder diffraction.

IT 810679-97-1
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES
(Uses)
(novel crystalline form of morpholin methylbenzamide derivative)

RN 810679-97-1 CAPLUS
CN Benzamide, 3,5-dibromo-N-[(2S)-2-(4-fluorophenyl)-4-[3-(4-morpholinyl)-1-azetidinyl]butyl]-N-methyl- (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 5 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

L4 ANSWER 6 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2007:382485 CAPLUS
DOCUMENT NUMBER: 146:379804
TITLE: Azetidine compounds as neurokinin receptor antagonists, their preparation, pharmaceutical compositions, and use in therapy
INVENTOR(S): Bergman, Rolf; Holmqvist, Sara; Von Unge, Sverker
PATENT ASSIGNEE(S): Astrazeneca AB, Swed.
SOURCE: PCT Int. Appl., 69pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007037743	A1	20070405	WO 2006-SE1092	20060927

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: SE 2005-2150 A 20050929

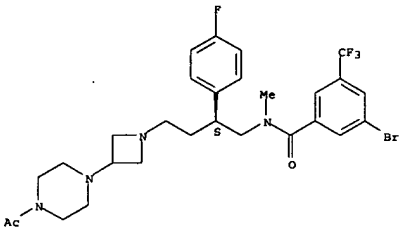
OTHER SOURCE(S): MARPAT 146:379804
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention relates to azetidine compds. of formula I, which are neurokinin (NK) receptor antagonists. In compds. I, Het is II or III; where Ar is 4-FC6H4; R is C1-4 alkyl, cyclopropyl, C1-4 methoxyalkyl, C1-4 ethoxyalkyl, C1-4 hydroxyalkyl, tetrahydrofuran-2-yl, tetrahydrofuran-3-yl, tetrahydropyran-2-yl, tetrahydropyran-3-yl, or tetrahydropyran-4-yl; and Y is C1-3 alkylene, -CH2OCH2-, or -CH2CH2O-; including salts and enantiomers thereof. The invention also relates to the the preparation of I, pharmaceutical compns. comprising a compound I as active ingredient and a pharmaceutically acceptable carrier or diluent, as well as to the use of the compns. for the treatment of functional gastrointestinal disorders, irritable bowel syndrome (IBS), and functional dyspepsia. Substitution of 1-(diphenylmethyl)-azetidin-3-yl methanesulfonate with pyrrolopyrazinone IV followed by deprotection gave azetidine V. Amidation of 3-bromo-5-trifluoromethylbenzoic acid with (S)-N-[2-(4-fluorophenyl)-pent-4-en-1-yl]methylamine resulted in the formation of benzamide VI, which underwent oxidation with osmium tetroxide and sodium periodate followed

L4 ANSWER 6 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
reductive amination with azetidine V to give the dihydrochloride of VII. The compds. of the invention are antagonists of NK receptors, e.g., compd.
VII expressed pKB values of 8.7, 7.8, and 8.5 for NK1, NK2, and NK3 receptors, resp.
IT 930783-06-5P 930783-07-6P, 3-Bromo-N-[(2S)-2-(4-fluorophenyl)-4-[3-(4-propionylpiperazin-1-yl)azetidin-1-yl]butyl]-N-methyl-5-(trifluoromethyl)benzamide dihydrochloride 930783-09-8P 930783-10-1P, 3-Bromo-N-[(2S)-2-(4-fluorophenyl)-4-[3-[4-(methoxyacetyl)piperazin-1-yl]azetidin-1-yl]butyl]-N-methyl-5-(trifluoromethyl)benzamide 930783-11-2P 930783-14-5P 930783-15-6P, 3-Bromo-N-[(2S)-4-[3-(4-butyrylpiperazin-1-yl)azetidin-1-yl]-2-(4-fluorophenyl)butyl]-N-methyl-5-(trifluoromethyl)benzamide dihydrochloride 930783-16-7P, 3-Bromo-N-[(2S)-2-(4-fluorophenyl)-4-[3-(4-isobutyrylpiperazin-1-yl)azetidin-1-yl]butyl]-N-methyl-5-(trifluoromethyl)benzamide dihydrochloride 930783-20-3P 930783-21-4P, 3-Bromo-N-[(2S)-4-[3-[4-(cyclopropylcarbonyl)piperazin-1-yl]azetidin-1-yl]-2-(4-fluorophenyl)butyl]-N-methyl-5-(trifluoromethyl)benzamide 930783-22-5P, 3-Bromo-N-[(2S)-4-[3-(4-butyrylpiperazin-1-yl)azetidin-1-yl]-2-(4-fluorophenyl)butyl]-N-methyl-5-(trifluoromethyl)benzamide 930783-23-6P, 3-Bromo-N-[(2S)-2-(4-fluorophenyl)-4-[3-(4-isobutyrylpiperazin-1-yl)azetidin-1-yl]butyl]-N-methyl-5-(trifluoromethyl)benzamide
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of azetidine derivs. as neurokinin receptor antagonists)
RN 930783-06-5 CAPLUS
CN Benzamide, N-[(2S)-4-[3-(4-acetyl-1-piperazinyl)-1-azetidinyl]-2-(4-fluorophenyl)butyl]-3-bromo-N-methyl-5-(trifluoromethyl)- (CA INDEX NAME)

Absolute stereochemistry.

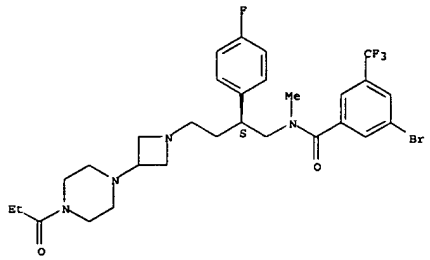


L4 ANSWER 6 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

RN 930783-07-6 CAPLUS
CN Benzamide, 3-bromo-N-[(2S)-2-(4-fluorophenyl)-4-[3-[4-(1-oxopropyl)-1-piperazinyl]-1-azetidinyl]butyl]-N-methyl-5-(trifluoromethyl)-, hydrochloride (1:2) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



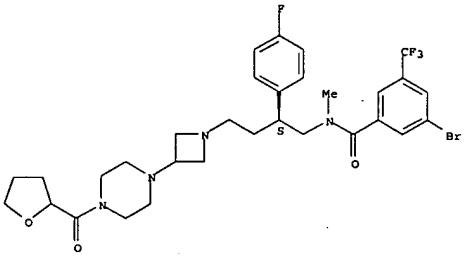
PAGE 2-A

●2 HCl

RN 930783-09-8 CAPLUS
CN Benzamide, 3-bromo-N-[(2S)-2-(4-fluorophenyl)-4-[3-[4-[(tetrahydro-2-furanyl)carbonyl]-1-piperazinyl]-1-azetidinyl]butyl]-N-methyl-5-(trifluoromethyl)- (CA INDEX NAME)

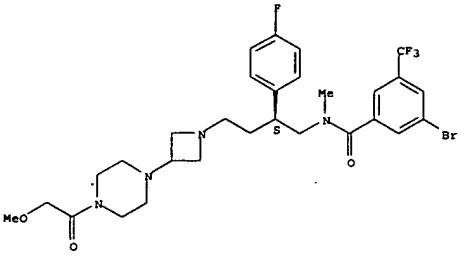
Absolute stereochemistry.

L4 ANSWER 6 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 930783-10-1 CAPLUS
CN Benzamide,
3-bromo-N-[(2S)-2-(4-fluorophenyl)-4-[3-[4-(2-methoxyacetyl)-1-piperazinyl]-1-azetidinyl]butyl]-N-methyl-5-(trifluoromethyl)- (CA INDEX NAME)

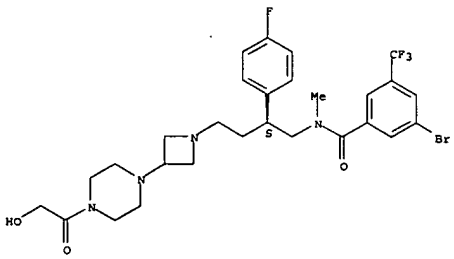
Absolute stereochemistry.



RN 930783-11-2 CAPLUS
CN Benzamide,
3-bromo-N-[(2S)-2-(4-fluorophenyl)-4-[3-[4-(2-hydroxyacetyl)-1-piperazinyl]-1-azetidinyl]butyl]-N-methyl-5-(trifluoromethyl)- (CA INDEX NAME)

Absolute stereochemistry.

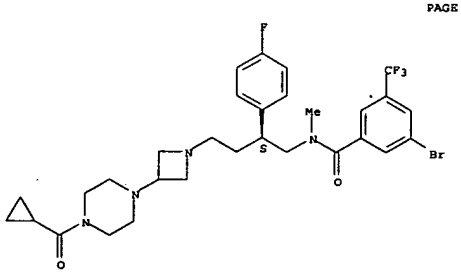
L4 ANSWER 6 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 930783-14-5 CAPLUS
CN Benzamide,
3-bromo-N-[(2S)-4-[3-[4-(cyclopropylcarbonyl)-1-piperazinyl]-1-azetidinyl]-2-(4-fluorophenyl)butyl]-N-methyl-5-(trifluoromethyl)-, hydrochloride (1:2) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 2-A

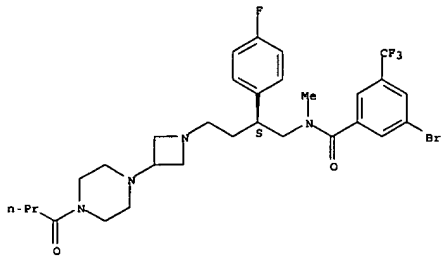
●2 HCl

RN 930783-15-6 CAPLUS
CN Benzamide, 3-bromo-N-[(2S)-2-(4-fluorophenyl)-4-[3-[4-(1-oxobutyl)-1-piperazinyl]-1-azetidinyl]butyl]-N-methyl-5-(trifluoromethyl)-,

L4 ANSWER 6 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
hydrochloride (1:2) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 2-A

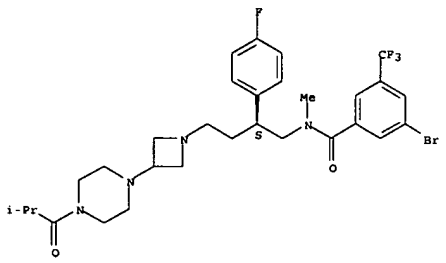
●2 HCl

RN 930783-16-7 CAPLUS
CN Benzamide, 3-bromo-N-[(2S)-2-(4-fluorophenyl)-4-[3-[4-(2-methyl-1-oxopropyl)-1-piperazinyl]-1-azetidinyl]butyl]-N-methyl-5-(trifluoromethyl)-, hydrochloride (1:2) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 6 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

PAGE 1-A

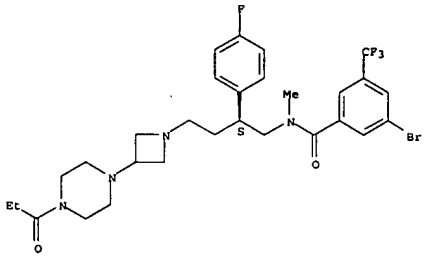


PAGE 2-A

●2 HCl

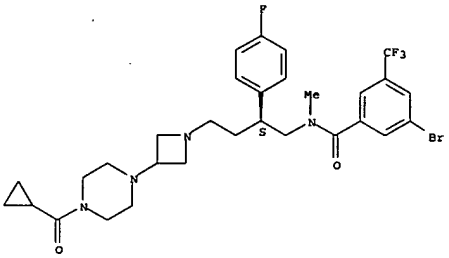
RN 930783-20-3 CAPLUS
CN Benzamide, 3-bromo-N-[(2S)-2-(4-fluorophenyl)-4-[3-[4-(1-oxopropyl)-1-piperazinyl]-1-azetidinyl]butyl]-N-methyl-5-(trifluoromethyl)- (CA INDEX NAME)

Absolute stereochemistry.



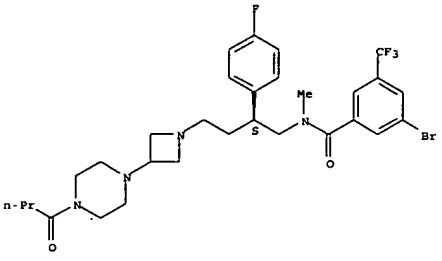
L4 ANSWER 6 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
RN 930783-21-4 CAPLUS
CN Benzamide, 3-bromo-N-[(2S)-4-[3-[4-(cyclopropylcarbonyl)-1-piperazinyl]-1-azetidinyl]-2-(4-fluorophenyl)butyl]-N-methyl-5-(trifluoromethyl)- (CA INDEX NAME)

Absolute stereochemistry.



RN 930783-22-5 CAPLUS
CN Benzamide, 3-bromo-N-[(2S)-2-(4-fluorophenyl)-4-[3-[4-(1-oxobutyl)-1-piperazinyl]-1-azetidinyl]butyl]-N-methyl-5-(trifluoromethyl)- (CA INDEX NAME)

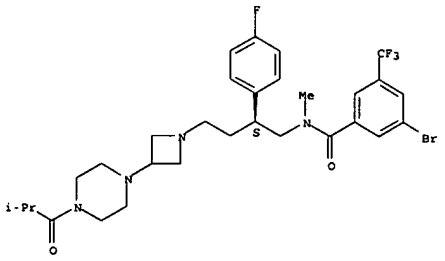
Absolute stereochemistry.



RN 930783-23-6 CAPLUS
CN Benzamide, 3-bromo-N-[(2S)-2-(4-fluorophenyl)-4-[3-[4-(2-methyl-1-oxopropyl)-1-piperazinyl]-1-azetidinyl]butyl]-N-methyl-5-(trifluoromethyl)-

L4 ANSWER 6 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
(CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L4 ANSWER 7 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:1356802 CAPLUS
DOCUMENT NUMBER: 146:100541
TITLE: Preparation of azetidine derivatives as neurokinin receptor antagonists for treatment of gastrointestinal diseases
INVENTOR(S): Holmqvist, Sara; Johansson, Anders; Svensson, Arne; Von Unge, Sverker
PATENT ASSIGNEE(S): Astrazeneca AB, Swed.
SOURCE: PCT Int. Appl., 53pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

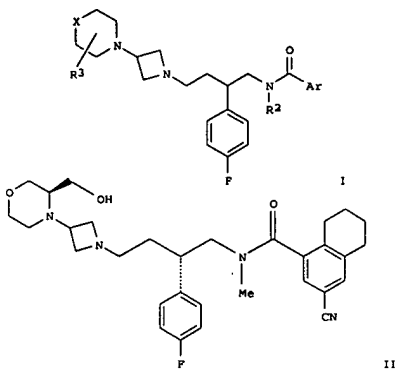
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006137790	A1	20061228	WO 2006-SE759	20060621

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: SE 2005-1494 A 20050623

OTHER SOURCE(S): MARPAT 146:100541
GI

L4 ANSWER 7 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



I

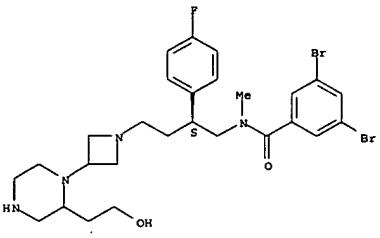
II

AB The title compds. with general formula I [wherein R2 = (un)substituted C1-4 alkyl; R3 = (CH2)nC(R6)(R7)OH, where n = 0-3; R6 and R7 = independently H or methyl; X = O or (un)substituted NH; Ar = substituted Ph, naphthyl, etc.] or pharmaceutically acceptable salts thereof are prepared as neurokinin receptor antagonists for the treatment of gastrointestinal diseases., For example, the compound II was prepared in a multi-step synthesis. II showed antagonistic activity with pKB value of 8.1, 7.6, and 7.1 against NK1, NK2, and NK3 receptors, resp. II also showed statistically significant CYP3A4 inhibitory activity with IC50 value of 19.2 μM.

IT 917572-08-8P 917572-11-3P 917572-12-4P
917572-14-6P 917572-15-7P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of azetidine derivs. as neurokinin receptor antagonists for treatment of gastrointestinal diseases)

RN 917572-08-8 CAPLUS
CN Benzamide, 3,5-dibromo-N-[(2S)-2-(4-fluorophenyl)-4-[3-[2-(2-hydroxyethyl)-1-piperazinyl]-1-azetidinyl]butyl]-N-methyl-, hydrochloride (1:3) (CA INDEX NAME)

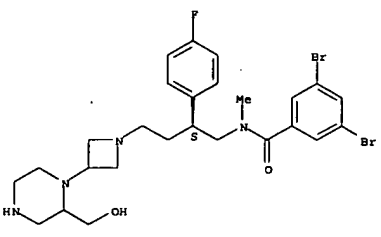
L4 ANSWER 7 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
Absolute stereochemistry.



●3 HCl

RN 917572-11-3 CAPLUS
CN Benzamide, 3,5-dibromo-N-[(2S)-2-(4-fluorophenyl)-4-[3-[2-(hydroxymethyl)-1-piperazinyl]-1-azetidinyl]butyl]-N-methyl-, hydrochloride (1:3) (CA INDEX NAME)

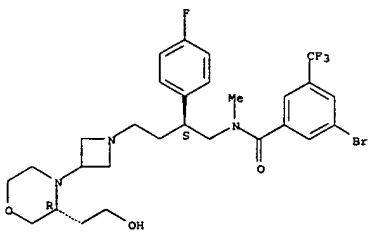
Absolute stereochemistry.



●3 HCl

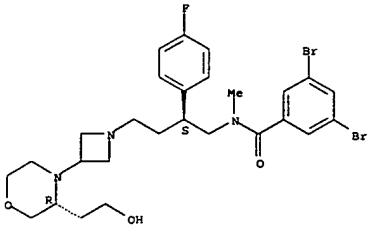
RN 917572-12-4 CAPLUS
CN Benzamide, 3-bromo-N-[(2S)-2-(4-fluorophenyl)-4-[3-[(3R)-3-(2-hydroxyethyl)-4-morpholinyl]-1-azetidinyl]butyl]-N-methyl-5-(trifluoromethyl)- (CA INDEX NAME)

L4 ANSWER 7 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
Absolute stereochemistry.



RN 917572-14-6 CAPLUS
CN Benzamide, 3,5-dibromo-N-[(2S)-2-(4-fluorophenyl)-4-[3-[(3R)-3-(2-hydroxyethyl)-4-morpholinyl]-1-azetidinyl]butyl]-N-methyl- (CA INDEX NAME)

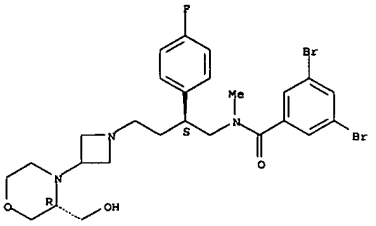
Absolute stereochemistry.



RN 917572-15-7 CAPLUS
CN Benzamide, 3,5-dibromo-N-[(2S)-2-(4-fluorophenyl)-4-[3-[(3R)-3-(hydroxymethyl)-4-morpholinyl]-1-azetidinyl]butyl]-N-methyl- (CA INDEX NAME)

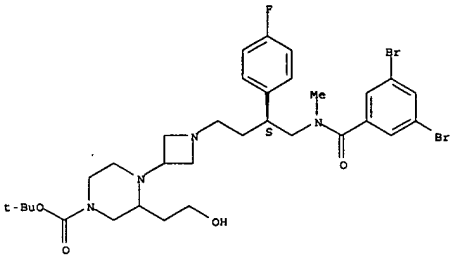
Absolute stereochemistry.

L4 ANSWER 7 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



IT 917572-17-9P 917572-24-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of azetidine deriva. as neurokinin receptor antagonists for
treatment of gastrointestinal diseases)
RN 917572-17-9 CAPLUS
CN 1-Piperazinecarboxylic acid, 4-[1-[(3S)-4-[(3,5-dibromobenzoyl)methylamino]-3-(4-fluorophenyl)butyl]-3-azetidinyl]-3-(2-hydroxyethyl)-, 1,1-dimethylethyl ester (CA INDEX NAME)

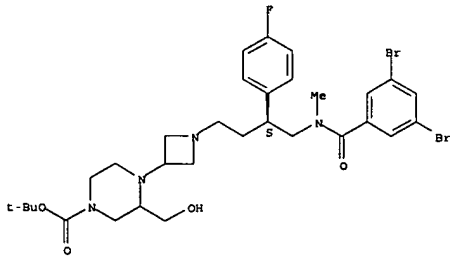
Absolute stereochemistry.



RN 917572-24-8 CAPLUS
CN 1-Piperazinecarboxylic acid, 4-[1-[(3S)-4-[(3,5-dibromobenzoyl)methylamino]-3-(4-fluorophenyl)butyl]-3-azetidinyl]-3-(hydroxymethyl)-, 1,1-dimethylethyl ester (CA INDEX NAME)

L4 ANSWER 7 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

Absolute stereochemistry.



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 8 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2006:1356559 CAPLUS
DOCUMENT NUMBER: 146:100540
TITLE: Preparation of azetidine derivatives as neurokinin receptor antagonists for treatment of gastrointestinal diseases
INVENTOR(S): Johansson, Anders; Johansson, Johan; Von Unge, Sverker
PATENT ASSIGNEE(S): Astrazeneca AB, Swed.
SOURCE: PCT Int. Appl., 76pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

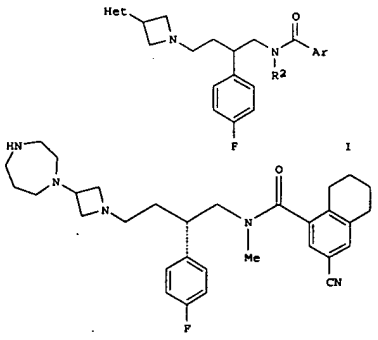
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006137791	A1	20061228	WO 2006-SE760	20060621

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: SE 2005-1493 A 20050623

OTHER SOURCE(S): MARPAT 146:100540
GI

L4 ANSWER 8 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

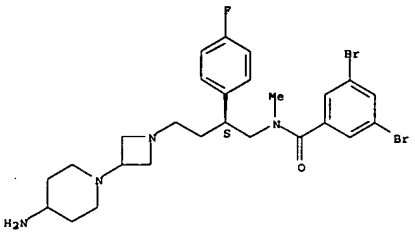


II

AB The title compds. with general formula I [wherein R2 = (un)substituted C1-4 alkyl; Het = 2,5-diazabicyclo[2.2.1]heptane, octahydropyrrolo[3,4-c]pyrrole, 1,4-diazepane, etc.; Ar = substituted Ph, naphthyl, etc.] or pharmaceutically acceptable salts thereof are prepared as neurokinin receptor antagonists for the treatment of gastrointestinal diseases. For example, the compound II was prepared in a multi-step synthesis. I showed antagonistic activity with pKB value of 7-9 against both NK1 and NK2 receptors, and pKB value of 6-9 against NK3 receptor. I also showed statistically significant CYP3A4 and hERG inhibitory activities with IC50 values of >2 μM and >10 μM, resp.
IT 917609-69-9P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of azetidine deriva. as neurokinin receptor antagonists for
treatment of gastrointestinal diseases)
RN 917609-69-9 CAPLUS
CN Benzamide, N-[(2S)-4-[3-(4-amino-1-piperidinyl)-1-azetidinyl]-2-(4-fluorophenyl)butyl]-3,5-dibromo-N-methyl-, hydrochloride (1:3) (CA INDEX NAME)

Absolute stereochemistry.

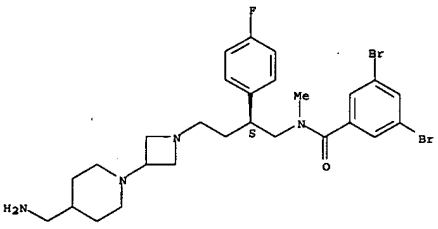
L4 ANSWER 8 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



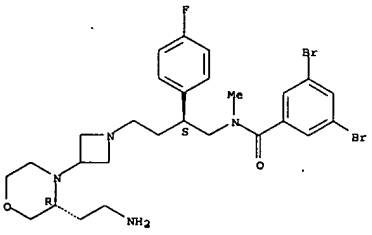
●3 HCl

IT 917609-70-2P 917609-72-4P 917609-73-5P
917609-79-1P 917609-83-7P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of azetidine derivs. as neurokinin receptor antagonists for
treatment of gastrointestinal diseases)
RN 917609-70-2 CAPLUS
CN Benzamide,
N-[(2S)-4-[3-[4-(aminomethyl)-1-piperidinyl]-1-azetidinyl]-2-(4-fluorophenyl)butyl]-3,5-dibromo-N-methyl- (CA INDEX NAME)

Absolute stereochemistry.

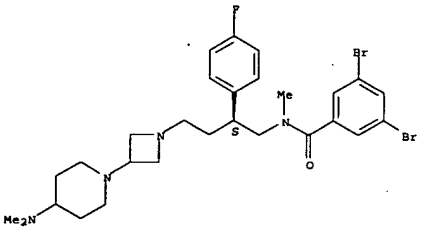


L4 ANSWER 8 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
Absolute stereochemistry.



RN 917609-83-7 CAPLUS
CN Benzamide, 3,5-dibromo-N-[(2S)-4-[3-[4-(dimethylamino)-1-piperidinyl]-1-azetidinyl]-2-(4-fluorophenyl)butyl]-N-methyl- (CA INDEX NAME)

Absolute stereochemistry.



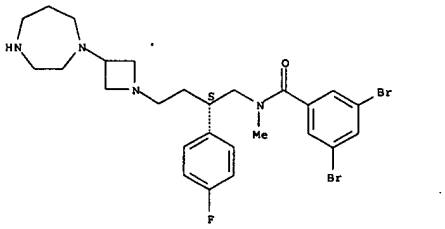
IT 917609-96-2P 917609-97-3P 917610-01-6P
917610-14-1P 917610-33-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of azetidine derivs. as neurokinin receptor antagonists for
treatment of gastrointestinal diseases)
RN 917609-96-2 CAPLUS
CN Carbamic acid, N-[1-[1-[(3S)-4-[(3,5-dibromobenzoyl)methylamino]-3-(4-fluorophenyl)butyl]-3-azetidinyl]-4-piperidinyl]-, 1,1-dimethylethyl ester
(CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 8 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

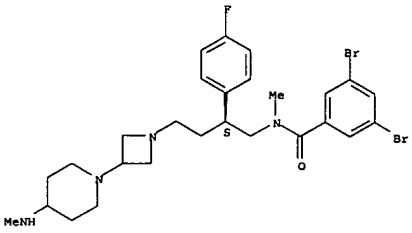
RN 917609-72-4 CAPLUS
CN Benzamide, 3,5-dibromo-N-[(2S)-2-(4-fluorophenyl)-4-[3-(hexahydro-1H-1,4-diazepin-1-yl)-1-azetidinyl]butyl]-N-methyl- (CA INDEX NAME)

Absolute stereochemistry.



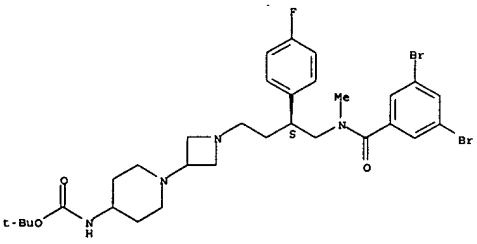
RN 917609-73-5 CAPLUS
CN Benzamide,
3,5-dibromo-N-[(2S)-2-(4-fluorophenyl)-4-[3-[4-(methylamino)-1-piperidinyl]-1-azetidinyl]butyl]-N-methyl- (CA INDEX NAME)

Absolute stereochemistry.



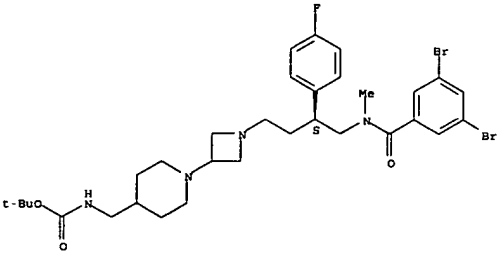
RN 917609-79-1 CAPLUS
CN Benzamide, N-[(2S)-4-[3-[(3R)-3-(2-aminoethyl)-4-morpholinyl]-1-azetidinyl]-2-(4-fluorophenyl)butyl]-3,5-dibromo-N-methyl- (CA INDEX NAME)

L4 ANSWER 8 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 917609-97-3 CAPLUS
CN Carbamic acid, N-[[1-[1-[(3S)-4-[(3,5-dibromobenzoyl)methylamino]-3-(4-fluorophenyl)butyl]-3-azetidinyl]-4-piperidinyl]methyl]-, 1,1-dimethylethyl ester (CA INDEX NAME)

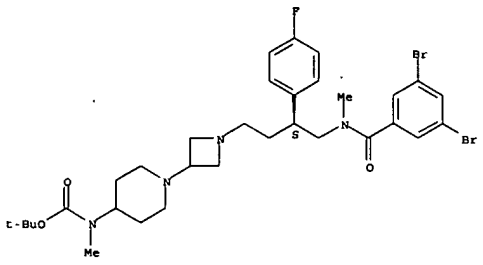
Absolute stereochemistry.



RN 917610-01-6 CAPLUS
CN Carbamic acid, N-[1-[1-[(3S)-4-[(3,5-dibromobenzoyl)methylamino]-3-(4-fluorophenyl)butyl]-3-azetidinyl]-4-piperidinyl]-N-methyl-, 1,1-dimethylethyl ester (CA INDEX NAME)

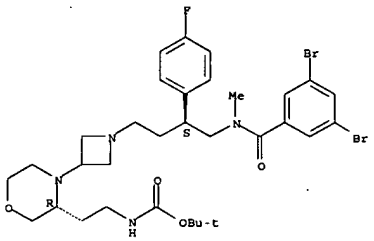
Absolute stereochemistry.

L4 ANSWER 8 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 917610-14-1 CAPLUS
CN Carbamic acid,
N-[2-[(3R)-4-(1-[(3S)-4-[(3,5-dibromobenzoyl)methylamino]-3-(4-fluorophenyl)butyl]-3-azetidinyl]-3-morpholinyl]ethyl]-, 1,1-dimethylethyl ester (CA INDEX NAME)

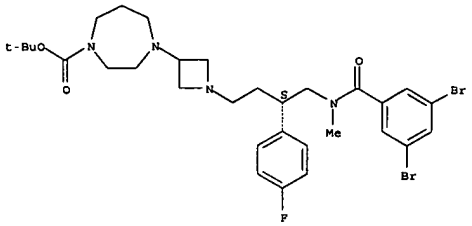
Absolute stereochemistry.



RN 917610-33-4 CAPLUS
CN 1H-1,4-Diazepine-1-carboxylic acid, 4-[1-[(3S)-4-[(3,5-dibromobenzoyl)methylamino]-3-(4-fluorophenyl)butyl]-3-azetidinyl]hexahydro-, 1,1-dimethylethyl ester (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 8 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 9 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2006:558670 CAPLUS
DOCUMENT NUMBER: 145:40270
TITLE: Dual NK1/NK2 receptor antagonists for the treatment of gastrointestinal disorders
INVENTOR(S): Astin Nielsen, Maria
PATENT ASSIGNEE(S): Astrazeneca AB, Swed.
SOURCE: PCT Int. Appl., 52 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006062478	A1	20060615	WO 2005-SE1866	20051207

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: SE 2004-3005 A 20041209

OTHER SOURCE(S): MARPAT 145:40270

AB The invention discloses the use of dual NK1/NK2 receptor antagonists for the treatment of functional gastrointestinal disorders, e.g. functional dyspepsia.

IT 810678-98-9 810678-98-9D, enantiomers and salts
810679-02-8 810679-02-8D, enantiomers and salts
810679-04-0 810679-04-0D, enantiomers and salts
810679-08-4 810679-08-4D, enantiomers and salts
810679-16-4 810679-16-4D, enantiomers and salts
810679-21-1 810679-21-1D, enantiomers and salts
810679-25-5 810679-25-5D, enantiomers and salts
810679-26-6 810679-26-6D, enantiomers and salts
810679-30-2 810679-30-2D, enantiomers and salts
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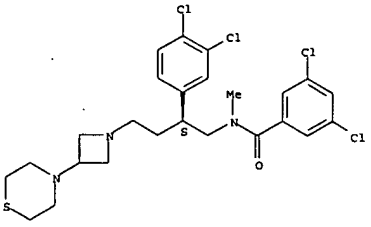
810679-33-5 810679-33-5D, enantiomers and salts
810679-54-0 810679-54-0D, enantiomers and salts
810679-62-0 810679-62-0D, enantiomers and salts
810679-64-2 810679-64-2D, enantiomers and salts
810679-72-2 810679-72-2D, enantiomers and salts
810679-76-6 810679-76-6D, enantiomers and salts
810679-97-1 810679-97-1D, enantiomers and salts
810680-24-1 810680-24-1D, enantiomers and salts
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(dual NK1/NK2 receptor antagonists for treatment of gastrointestinal disorders)

RN 810678-98-9 CAPLUS
CN Benzamide, 3,5-dichloro-N-[(2S)-2-(3,4-dichlorophenyl)-4-[3-(4-thiomorpholinyl)-1-azetidinyl]butyl]-N-methyl- (CA INDEX NAME)

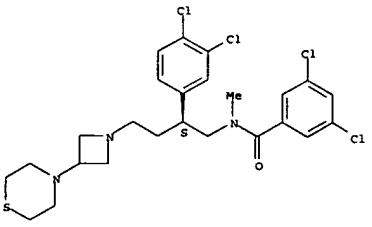
Absolute stereochemistry.

L4 ANSWER 9 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 810678-98-9 CAPLUS
CN Benzamide, 3,5-dichloro-N-[(2S)-2-(3,4-dichlorophenyl)-4-[3-(4-thiomorpholinyl)-1-azetidinyl]butyl]-N-methyl- (CA INDEX NAME)

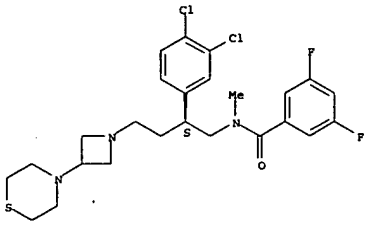
Absolute stereochemistry.



RN 810679-02-8 CAPLUS
CN Benzamide, N-[(2S)-2-(3,4-dichlorophenyl)-4-[3-(4-thiomorpholinyl)-1-azetidinyl]butyl]-3,5-difluoro-N-methyl- (CA INDEX NAME)

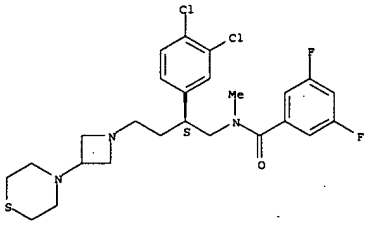
Absolute stereochemistry.

L4 ANSWER 9 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 810679-02-8 CAPLUS
CN Benzamide, N-[(2S)-2-(3,4-dichlorophenyl)-4-[3-(4-thiomorpholinyl)-1-azetidinyl]butyl]-3,5-difluoro-N-methyl- (CA INDEX NAME)

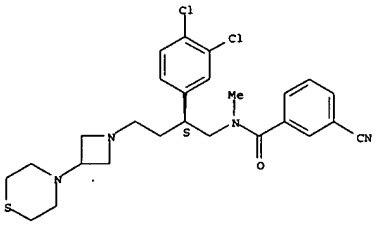
Absolute stereochemistry.



RN 810679-04-0 CAPLUS
CN Benzamide, N-[(2S)-2-(3,4-dichlorophenyl)-4-[3-(4-thiomorpholinyl)-1-azetidinyl]butyl]-N-methyl-3,5-bis(trifluoromethyl)- (CA INDEX NAME)

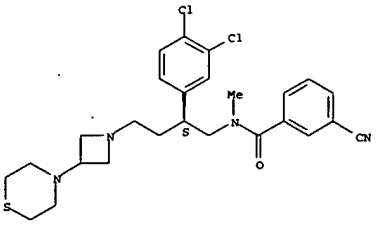
Absolute stereochemistry.

L4 ANSWER 9 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 810679-08-4 CAPLUS
CN Benzamide,
3-cyano-N-[(2S)-2-(3,4-dichlorophenyl)-4-[3-(4-thiomorpholinyl)-1-azetidinyl]butyl]-N-methyl- (CA INDEX NAME)

Absolute stereochemistry.



RN 810679-16-4 CAPLUS
CN Benzamide, N-[2-(4-fluorophenyl)-4-[3-(4-thiomorpholinyl)-1-azetidinyl]butyl]-N-methyl-3,5-bis(trifluoromethyl)- (CA INDEX NAME)

L4 ANSWER 9 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

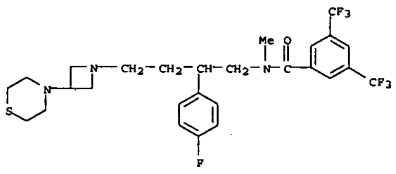
RN 810679-04-0 CAPLUS
CN Benzamide, N-[(2S)-2-(3,4-dichlorophenyl)-4-[3-(4-thiomorpholinyl)-1-azetidinyl]butyl]-N-methyl-3,5-bis(trifluoromethyl)- (CA INDEX NAME)

Absolute stereochemistry.

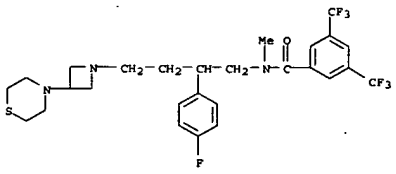
RN 810679-08-4 CAPLUS
CN Benzamide,
3-cyano-N-[(2S)-2-(3,4-dichlorophenyl)-4-[3-(4-thiomorpholinyl)-1-azetidinyl]butyl]-N-methyl- (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 9 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

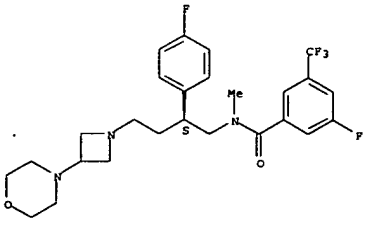


RN 810679-16-4 CAPLUS
CN Benzamide, N-[2-(4-fluorophenyl)-4-[3-(4-thiomorpholinyl)-1-azetidinyl]butyl]-N-methyl-3,5-bis(trifluoromethyl)- (CA INDEX NAME)



RN 810679-21-1 CAPLUS
CN Benzamide, 3-fluoro-N-[(2S)-2-(4-fluorophenyl)-4-[3-(4-morpholinyl)-1-azetidinyl]butyl]-N-methyl-5-(trifluoromethyl)- (CA INDEX NAME)

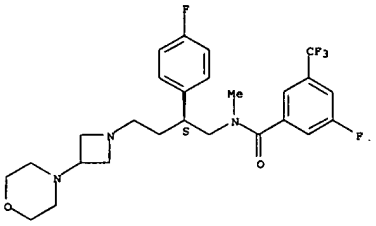
Absolute stereochemistry.



RN 810679-21-1 CAPLUS

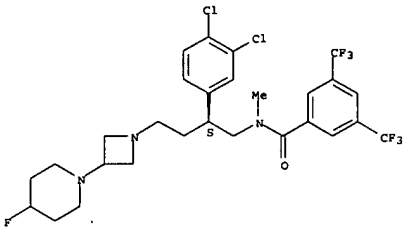
L4 ANSWER 9 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
CN Benzamide, 3-fluoro-N-[(2S)-2-(4-fluorophenyl)-4-[3-(4-morpholinyl)-1-azetidinyl]butyl]-N-methyl-5-(trifluoromethyl)- (CA INDEX NAME)

Absolute stereochemistry.



RN 810679-25-5 CAPLUS
CN Benzamide,
N-[(2S)-2-(3,4-dichlorophenyl)-4-[3-(4-fluoro-1-piperidinyl)-1-azetidinyl]butyl]-N-methyl-3,5-bis(trifluoromethyl)- (CA INDEX NAME)

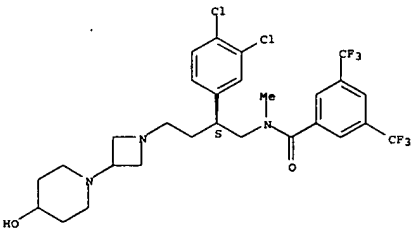
Absolute stereochemistry.



RN 810679-25-5 CAPLUS
CN Benzamide,
N-[(2S)-2-(3,4-dichlorophenyl)-4-[3-(4-fluoro-1-piperidinyl)-1-azetidinyl]butyl]-N-methyl-3,5-bis(trifluoromethyl)- (CA INDEX NAME)

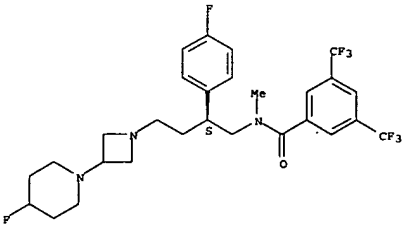
Absolute stereochemistry.

L4 ANSWER 9 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 810679-30-2 CAPLUS
CN Benzamide, N-[(2S)-2-(4-fluorophenyl)-4-[3-(4-fluoro-1-piperidinyl)-1-azetidinyl]butyl]-N-methyl-3,5-bis(trifluoromethyl)- (CA INDEX NAME)

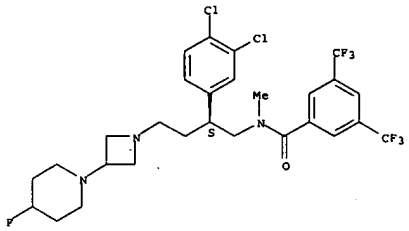
Absolute stereochemistry.



RN 810679-30-2 CAPLUS
CN Benzamide, N-[(2S)-2-(4-fluorophenyl)-4-[3-(4-fluoro-1-piperidinyl)-1-azetidinyl]butyl]-N-methyl-3,5-bis(trifluoromethyl)- (CA INDEX NAME)

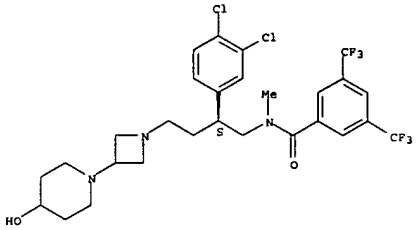
Absolute stereochemistry.

L4 ANSWER 9 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 810679-26-6 CAPLUS
CN Benzamide,
N-[(2S)-2-(3,4-dichlorophenyl)-4-[3-(4-hydroxy-1-piperidinyl)-1-azetidinyl]butyl]-N-methyl-3,5-bis(trifluoromethyl)- (CA INDEX NAME)

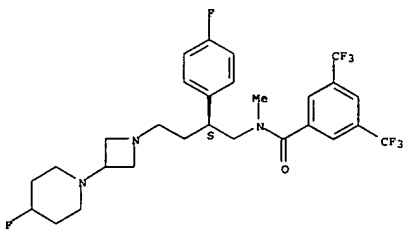
Absolute stereochemistry.



RN 810679-26-6 CAPLUS
CN Benzamide,
N-[(2S)-2-(3,4-dichlorophenyl)-4-[3-(4-hydroxy-1-piperidinyl)-1-azetidinyl]butyl]-N-methyl-3,5-bis(trifluoromethyl)- (CA INDEX NAME)

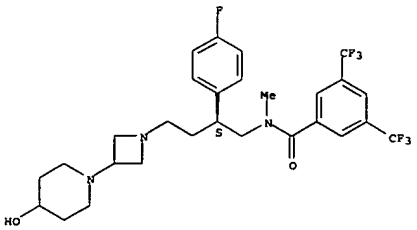
Absolute stereochemistry.

L4 ANSWER 9 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 810679-32-4 CAPLUS
CN Benzamide, N-[(2S)-2-(4-fluorophenyl)-4-[3-(4-hydroxy-1-piperidinyl)-1-azetidinyl]butyl]-N-methyl-3,5-bis(trifluoromethyl)- (CA INDEX NAME)

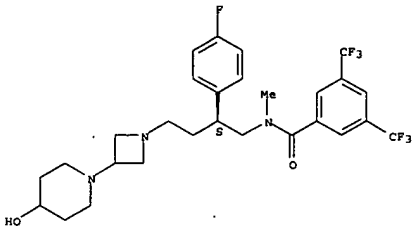
Absolute stereochemistry.



RN 810679-32-4 CAPLUS
CN Benzamide, N-[(2S)-2-(4-fluorophenyl)-4-[3-(4-hydroxy-1-piperidinyl)-1-azetidinyl]butyl]-N-methyl-3,5-bis(trifluoromethyl)- (CA INDEX NAME)

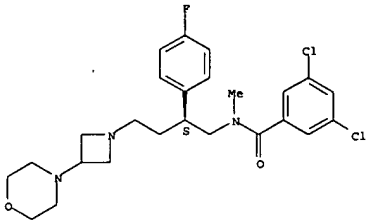
Absolute stereochemistry.

L4 ANSWER 9 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 810679-33-5 CAPLUS
CN Benzamide,
3,5-dichloro-N-[(2S)-2-(4-fluorophenyl)-4-[3-(4-morpholinyl)-1-azetidinyl]butyl]-N-methyl- (CA INDEX NAME)

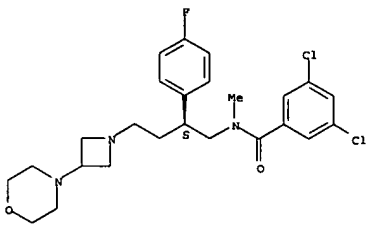
Absolute stereochemistry.



RN 810679-33-5 CAPLUS
CN Benzamide,
3,5-dichloro-N-[(2S)-2-(4-fluorophenyl)-4-[3-(4-morpholinyl)-1-azetidinyl]butyl]-N-methyl- (CA INDEX NAME)

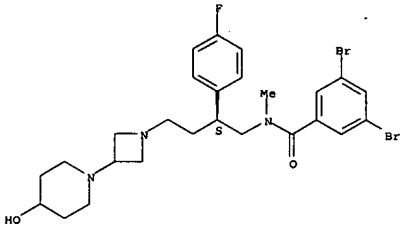
Absolute stereochemistry.

L4 ANSWER 9 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 810679-54-0 CAPLUS
CN Benzamide, 3,5-dibromo-N-[(2S)-2-(4-fluorophenyl)-4-[3-(4-hydroxy-1-piperidinyl)-1-azetidinyl]butyl]-N-methyl- (CA INDEX NAME)

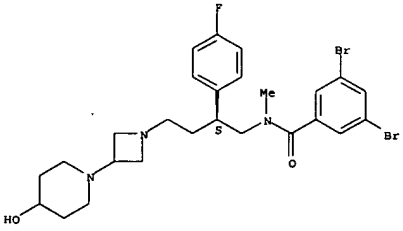
Absolute stereochemistry.



RN 810679-54-0 CAPLUS
CN Benzamide, 3,5-dibromo-N-[(2S)-2-(4-fluorophenyl)-4-[3-(4-hydroxy-1-piperidinyl)-1-azetidinyl]butyl]-N-methyl- (CA INDEX NAME)

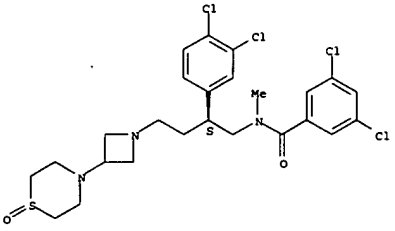
Absolute stereochemistry.

L4 ANSWER 9 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 810679-62-0 CAPLUS
CN Benzamide, 3,5-dichloro-N-[(2S)-2-(3,4-dichlorophenyl)-4-[3-(1-oxido-4-thiomorpholinyl)-1-azetidinyl]butyl]-N-methyl- (CA INDEX NAME)

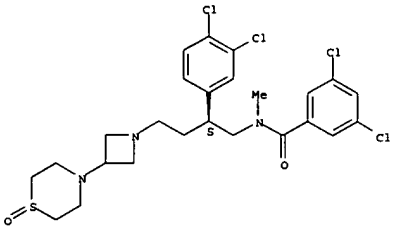
Absolute stereochemistry.



RN 810679-62-0 CAPLUS
CN Benzamide, 3,5-dichloro-N-[(2S)-2-(3,4-dichlorophenyl)-4-[3-(1-oxido-4-thiomorpholinyl)-1-azetidinyl]butyl]-N-methyl- (CA INDEX NAME)

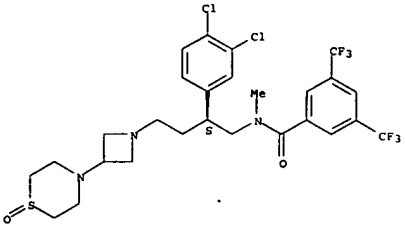
Absolute stereochemistry.

L4 ANSWER 9 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 810679-64-2 CAPLUS
CN Benzamide,
N-[(2S)-2-(3,4-dichlorophenyl)-4-[3-(1-oxido-4-thiomorpholinyl)-1-azetidinyl]butyl]-N-methyl-3,5-bis(trifluoromethyl)- (CA INDEX NAME)

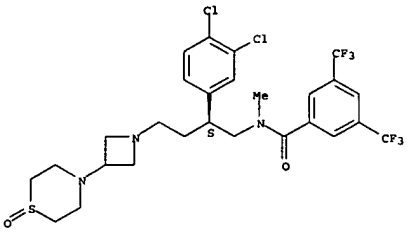
Absolute stereochemistry.



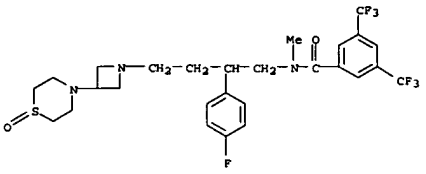
RN 810679-64-2 CAPLUS
CN Benzamide,
N-[(2S)-2-(3,4-dichlorophenyl)-4-[3-(1-oxido-4-thiomorpholinyl)-1-azetidinyl]butyl]-N-methyl-3,5-bis(trifluoromethyl)- (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 9 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



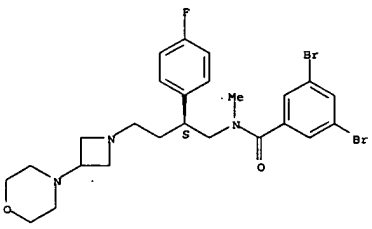
RN 810679-72-2 CAPLUS
CN Benzamide, N-[2-(4-fluorophenyl)-4-[3-(1-oxido-4-thiomorpholinyl)-1-azetidinyl]butyl]-N-methyl-3,5-bis(trifluoromethyl)- (CA INDEX NAME)



RN 810679-72-2 CAPLUS
CN Benzamide, N-[2-(4-fluorophenyl)-4-[3-(1-oxido-4-thiomorpholinyl)-1-azetidinyl]butyl]-N-methyl-3,5-bis(trifluoromethyl)- (CA INDEX NAME)

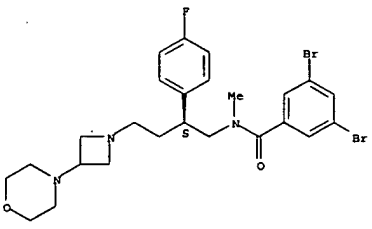
L4 ANSWER 9 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
azetidinyl]butyl]-N-methyl- (CA INDEX NAME)

Absolute stereochemistry.



RN 810679-97-1 CAPLUS
CN Benzamide, 3,5-dibromo-N-[(2S)-2-(4-fluorophenyl)-4-[3-(4-morpholinyl)-1-azetidinyl]butyl]-N-methyl- (CA INDEX NAME)

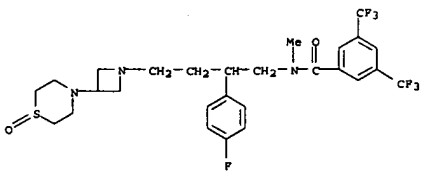
Absolute stereochemistry.



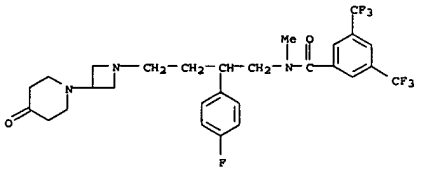
RN 810680-24-1 CAPLUS
CN Benzamide, 3-bromo-N-[(2S)-2-(4-fluorophenyl)-4-[3-(4-morpholinyl)-1-azetidinyl]butyl]-5-iodo-N-methyl- (CA INDEX NAME)

Absolute stereochemistry.

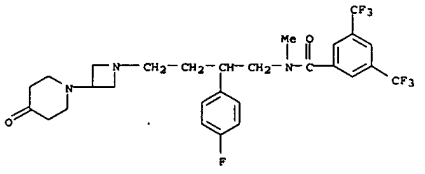
L4 ANSWER 9 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 810679-76-6 CAPLUS
CN Benzamide, N-[2-(4-fluorophenyl)-4-[3-(4-oxo-1-piperidinyl)-1-azetidinyl]butyl]-N-methyl-3,5-bis(trifluoromethyl)- (CA INDEX NAME)

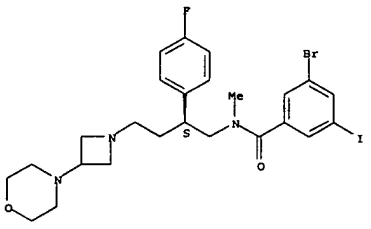


RN 810679-76-6 CAPLUS
CN Benzamide, N-[2-(4-fluorophenyl)-4-[3-(4-oxo-1-piperidinyl)-1-azetidinyl]butyl]-N-methyl-3,5-bis(trifluoromethyl)- (CA INDEX NAME)



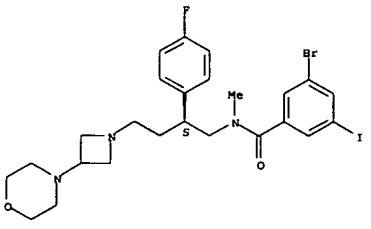
RN 810679-97-1 CAPLUS
CN Benzamide, 3,5-dibromo-N-[(2S)-2-(4-fluorophenyl)-4-[3-(4-morpholinyl)-1-

L4 ANSWER 9 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 810680-24-1 CAPLUS
CN Benzamide, 3-bromo-N-[(2S)-2-(4-fluorophenyl)-4-[3-(4-morpholinyl)-1-azetidinyl]butyl]-5-iodo-N-methyl- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

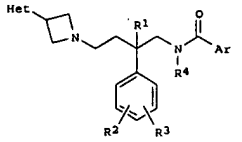
FORMAT

L4 ANSWER 10 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:1124562 CAPLUS
DOCUMENT NUMBER: 142:56156
TITLE: Preparation of heterocyclic-substituted azetidines as NK1/NK2 receptor antagonists
INVENTOR(S): Johansson, Anders; Persson, Joachim
PATENT ASSIGNEE(S): Astrazeneca Ab, Swed.
SOURCE: PCT Int. Appl., 107 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004110344	A2	20041223	WO 2004-SE901	20040609
WO 2004110344	A3	20050217		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2004246983	A1	20041223	AU 2004-246983	20040609
CA 2529126	A1	20041223	CA 2004-2529126	20040609
EP 1636221	A2	20060322	EP 2004-736475	20040609
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR				
CN 1805957	A	20060719	CN 2004-80016343	20040609
BR 2004011285	A	20060801	BR 2004-11285	20040609
JP 2006527267	T	20061130	JP 2006-517025	20040609
MX 2005PA13276	A	20060309	MX 2005-PA13276	20051207
US 2006172988	A1	20060803	US 2005-560319	20051209
NO 2006000206	A	20060313	NO 2006-206	20060113
PRIORITY APPLN. INFO.:			SE 2003-1744 A	20030613
			SE 2003-3493 A	20031219
			WO 2004-SE901 W	20040609

OTHER SOURCE(S): CASREACT 142:56156; MARPAT 142:56156
GI

L4 ANSWER 10 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



I

AB Title compds. I (Het = (un)substituted 4-7-membered heterocycle; R1 = H, OH, alkyl, etc.; R2-3 = H, alkyl, cycloalkyl, alkenyl, alkynyl, etc.; R4 = alkyl, cycloalkyl, alkenyl, alkynyl; Ar = pyridinyl, naphthyl, etc.] are prepared For instance, 3,5-Dichloro-N-[(2S)-2-(3,4-dichlorophenyl)-4-(3-(thiomorpholin-4-yl)azetidin-1-yl)butyl]-N-methylbenzamide is prepared in 5 steps from 1-(diphenylmethyl)azetidine-3-yl methanesulfonate, thiomorpholine, tert-Bu [(2S)-2-(3,4-dichlorophenyl)-4-oxobutyl]methylcarbamate and 3,5-dichlorobenzoic acid. Example compds. exhibit pKB 7-9 for the NK1 and NK2 receptor and < 7.5 for the NK3 receptor. I are useful for the treatment of pain, depression, etc.
IT 810678-98-9P 810678-99-0P 810679-01-7P
810679-02-8P 810679-03-9P 810679-04-0P
810679-05-1P 810679-08-4P 810679-09-5P
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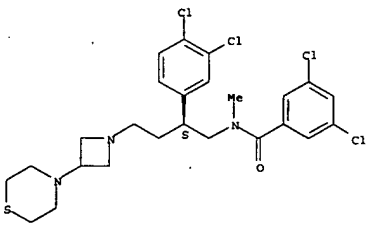
810679-54-0P 810679-55-1P 810679-62-0P
810679-63-1P 810679-64-2P 810679-65-3P
810679-72-2P 810679-73-3P 810679-76-6P
810679-97-1P 810680-24-1P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of heterocyclic-substituted azetidines as NK1/NK2 receptor antagonists)
RN 810678-98-9 CAPLUS
CN Benzamide, 3,5-dichloro-N-[(2S)-2-(3,4-dichlorophenyl)-4-[3-(4-thiomorpholinyl)-1-azetidinyl]butyl]-N-methyl- (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 10 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

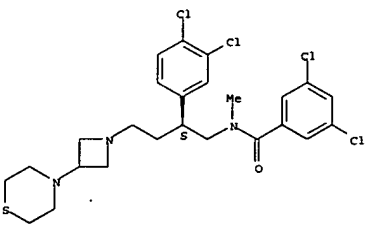


RN 810678-99-0 CAPLUS
CN Benzamide, 3,5-dichloro-N-[(2S)-2-(3,4-dichlorophenyl)-4-[3-(4-thiomorpholinyl)-1-azetidinyl]butyl]-N-methyl-, monoacetate (9CI) (CA INDEX NAME)

CM 1

CRN 810678-98-9
CMF C25 H29 Cl4 N3 O S

Absolute stereochemistry.



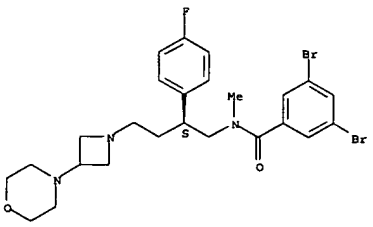
CM 2

CRN 64-19-7
CMF C2 H4 O2

L4 ANSWER 10 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

RN 810679-01-7 CAPLUS
CN Benzamide, 3,5-dibromo-N-[(2S)-2-(4-fluorophenyl)-4-[3-(4-morpholinyl)-1-azetidinyl]butyl]-N-methyl-, dihydrochloride (9CI) (CA INDEX NAME)

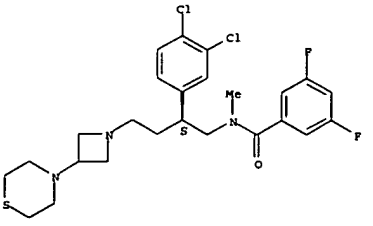
Absolute stereochemistry.



● 2 HCl

RN 810679-02-8 CAPLUS
CN Benzamide, N-[(2S)-2-(3,4-dichlorophenyl)-4-[3-(4-thiomorpholinyl)-1-azetidinyl]butyl]-3,5-difluoro-N-methyl- (CA INDEX NAME)

Absolute stereochemistry.



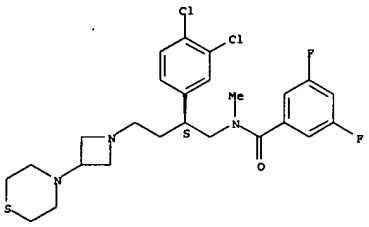
RN 810679-03-9 CAPLUS

L4 ANSWER 10 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
CN Benzamide, N-[(2S)-2-(3,4-dichlorophenyl)-4-[3-(4-thiomorpholinyl)-1-azetidinyl]butyl]-3,5-difluoro-N-methyl-, monoacetate (9CI) (CA INDEX NAME)

CM 1

CRN 810679-02-8
CMF C25 H29 Cl2 F2 N3 O S

Absolute stereochemistry.



CM 2

CRN 64-19-7
CMF C2 H4 O2

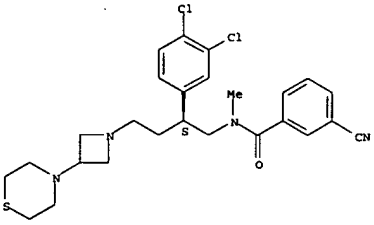
RN 810679-04-0 CAPLUS
CN Benzamide, N-[(2S)-2-(3,4-dichlorophenyl)-4-[3-(4-thiomorpholinyl)-1-azetidinyl]butyl]-N-methyl-3,5-bis(trifluoromethyl)- (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 10 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

RN 810679-08-4 CAPLUS
CN Benzamide,
3-cyano-N-[(2S)-2-(3,4-dichlorophenyl)-4-[3-(4-thiomorpholinyl)-1-azetidinyl]butyl]-N-methyl- (CA INDEX NAME)

Absolute stereochemistry.



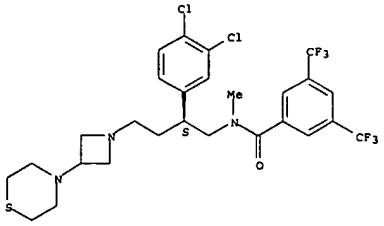
RN 810679-09-5 CAPLUS
CN Benzamide,
3-cyano-N-[(2S)-2-(3,4-dichlorophenyl)-4-[3-(4-thiomorpholinyl)-1-azetidinyl]butyl]-N-methyl-, monoacetate (9CI) (CA INDEX NAME)

CM 1

CRN 810679-08-4
CMF C26 H30 Cl2 N4 O S

Absolute stereochemistry.

L4 ANSWER 10 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

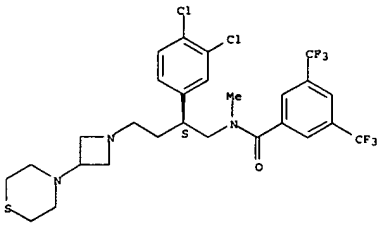


RN 810679-05-1 CAPLUS
CN Benzamide, N-[(2S)-2-(3,4-dichlorophenyl)-4-[3-(4-thiomorpholinyl)-1-azetidinyl]butyl]-N-methyl-3,5-bis(trifluoromethyl)-, monoacetate (9CI) (CA INDEX NAME)

CM 1

CRN 810679-04-0
CMF C27 H29 Cl2 F6 N3 O S

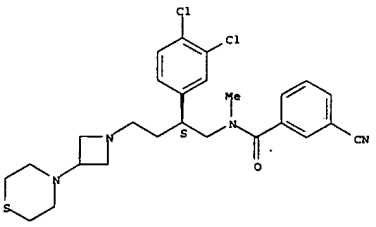
Absolute stereochemistry.



CM 2

CRN 64-19-7
CMF C2 H4 O2

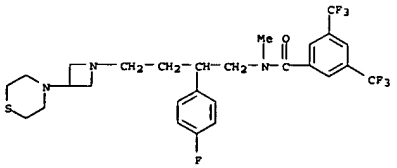
L4 ANSWER 10 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



CM 2

CRN 64-19-7
CMF C2 H4 O2

RN 810679-16-4 CAPLUS
CN Benzamide, N-[2-(4-fluorophenyl)-4-[3-(4-thiomorpholinyl)-1-azetidinyl]butyl]-N-methyl-3,5-bis(trifluoromethyl)- (CA INDEX NAME)

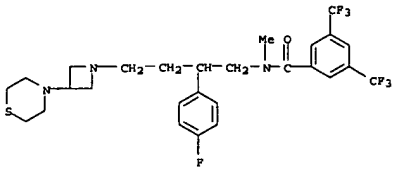


RN 810679-17-5 CAPLUS
CN Benzamide, N-[2-(4-fluorophenyl)-4-[3-(4-thiomorpholinyl)-1-azetidinyl]butyl]-N-methyl-3,5-bis(trifluoromethyl)-, diacetate (9CI) (CA
INDEX NAME)

CM 1

CRN 810679-16-4

L4 ANSWER 10 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
CMF C27 H30 F7 N3 O S

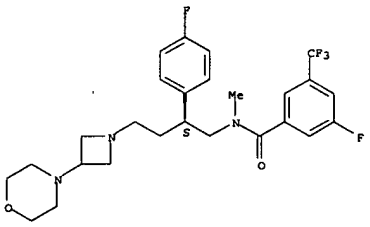


CM 2

CRN 64-19-7
CMF C2 H4 O2

RN 810679-21-1 CAPLUS
CN Benzamide, 3-fluoro-N-[(2S)-2-(4-fluorophenyl)-4-[3-(4-morpholinyl)-1-azetidinyl]butyl]-N-methyl-5-(trifluoromethyl)- (CA INDEX NAME)

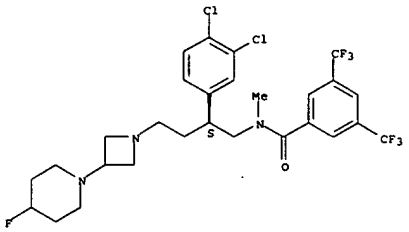
Absolute stereochemistry.



RN 810679-25-5 CAPLUS
CN Benzamide,
N-[(2S)-2-(3,4-dichlorophenyl)-4-[3-(4-fluoro-1-piperidinyl)-1-

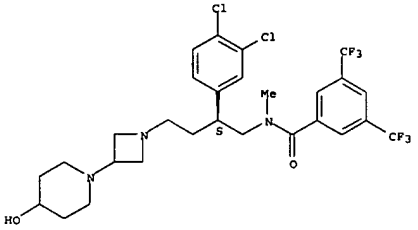
L4 ANSWER 10 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
azetidinyl]butyl]-N-methyl-3,5-bis(trifluoromethyl)- (CA INDEX NAME)

Absolute stereochemistry.



RN 810679-26-6 CAPLUS
CN Benzamide,
N-[(2S)-2-(3,4-dichlorophenyl)-4-[3-(4-hydroxy-1-piperidinyl)-1-azetidinyl]butyl]-N-methyl-3,5-bis(trifluoromethyl)- (CA INDEX NAME)

Absolute stereochemistry.

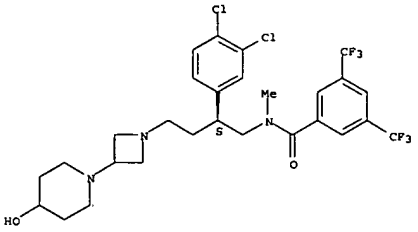


RN 810679-27-7 CAPLUS
CN Benzamide,
N-[(2S)-2-(3,4-dichlorophenyl)-4-[3-(4-hydroxy-1-piperidinyl)-1-azetidinyl]butyl]-N-methyl-3,5-bis(trifluoromethyl)-, diacetate (salt) (9CI) (CA INDEX NAME)

CM 1

L4 ANSWER 10 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
CRN 810679-26-6
CMF C28 H31 Cl2 F6 N3 O2

Absolute stereochemistry.

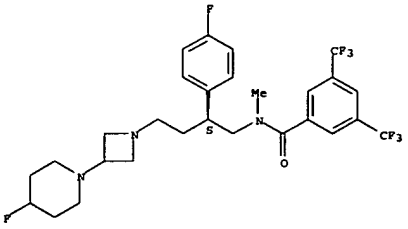


CM 2

CRN 64-19-7
CMF C2 H4 O2

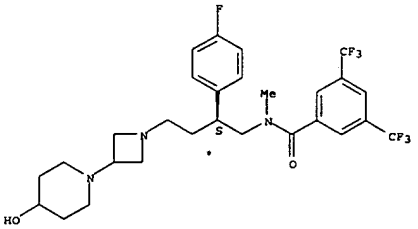
RN 810679-30-2 CAPLUS
CN Benzamide, N-[(2S)-2-(4-fluorophenyl)-4-[3-(4-fluoro-1-piperidinyl)-1-azetidinyl]butyl]-N-methyl-3,5-bis(trifluoromethyl)- (CA INDEX NAME)

Absolute stereochemistry.



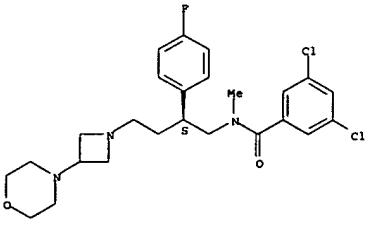
L4 ANSWER 10 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
RN 810679-32-4 CAPLUS
CN Benzamide, N-[(2S)-2-(4-fluorophenyl)-4-[3-(4-hydroxy-1-piperidinyl)-1-azetidinyl]butyl]-N-methyl-3,5-bis(trifluoromethyl)- (CA INDEX NAME)

Absolute stereochemistry.



RN 810679-33-5 CAPLUS
CN Benzamide,
3,5-dichloro-N-[(2S)-2-(4-fluorophenyl)-4-[3-(4-morpholinyl)-1-azetidinyl]butyl]-N-methyl- (CA INDEX NAME)

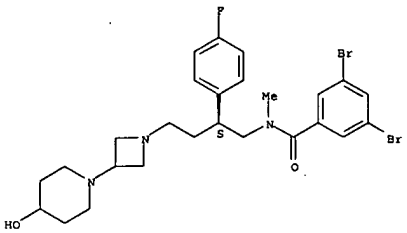
Absolute stereochemistry.



RN 810679-54-0 CAPLUS
CN Benzamide, 3,5-dibromo-N-[(2S)-2-(4-fluorophenyl)-4-[3-(4-hydroxy-1-piperidinyl)-1-azetidinyl]butyl]-N-methyl- (CA INDEX NAME)

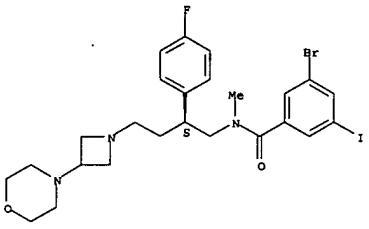
Absolute stereochemistry.

L4 ANSWER 10 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 810679-55-1 CAPLUS
CN Benzamide, 3-bromo-N-[(2S)-2-(4-fluorophenyl)-4-[3-(4-morpholinyl)-1-azetidinyl]butyl]-5-iodo-N-methyl-, dihydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.



●2 HCl

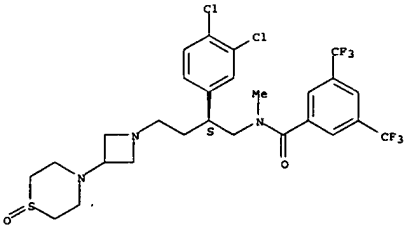
RN 810679-62-0 CAPLUS
CN Benzamide, 3,5-dichloro-N-[(2S)-2-(3,4-dichlorophenyl)-4-[3-(1-oxido-4-thiomorpholinyl)-1-azetidinyl]butyl]-N-methyl- (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 10 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

RN 810679-64-2 CAPLUS
CN Benzamide,
N-[(2S)-2-(3,4-dichlorophenyl)-4-[3-(1-oxido-4-thiomorpholinyl)-1-azetidinyl]butyl]-N-methyl-3,5-bis(trifluoromethyl)- (CA INDEX NAME)

Absolute stereochemistry.



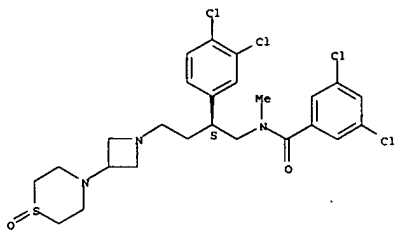
RN 810679-65-3 CAPLUS
CN Benzamide,
N-[(2S)-2-(3,4-dichlorophenyl)-4-[3-(1-oxido-4-thiomorpholinyl)-1-azetidinyl]butyl]-N-methyl-3,5-bis(trifluoromethyl)-, monoacetate (9CI) (CA INDEX NAME)

CM 1

CRN 810679-64-2
CMF C27 H29 Cl2 F6 N3 O2 S

Absolute stereochemistry.

L4 ANSWER 10 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

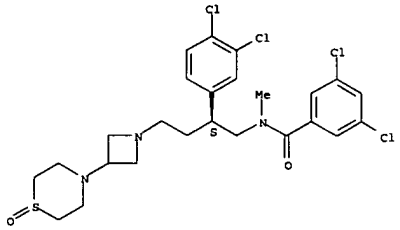


RN 810679-63-1 CAPLUS
CN Benzamide, 3,5-dichloro-N-[(2S)-2-(3,4-dichlorophenyl)-4-[3-(1-oxido-4-thiomorpholinyl)-1-azetidinyl]butyl]-N-methyl-, monoacetate (9CI) (CA INDEX NAME)

CM 1

CRN 810679-62-0
CMF C25 H29 Cl4 N3 O2 S

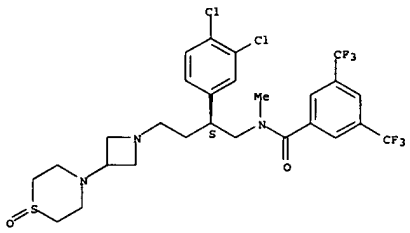
Absolute stereochemistry.



CM 2

CRN 64-19-7
CMF C2 H4 O2

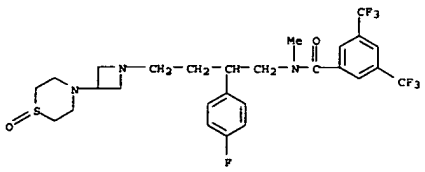
L4 ANSWER 10 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



CM 2

CRN 64-19-7
CMF C2 H4 O2

RN 810679-72-2 CAPLUS
CN Benzamide, N-[2-(4-fluorophenyl)-4-[3-(1-oxido-4-thiomorpholinyl)-1-azetidinyl]butyl]-N-methyl-3,5-bis(trifluoromethyl)- (CA INDEX NAME)

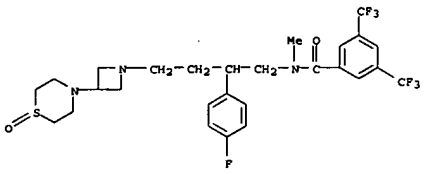


RN 810679-73-3 CAPLUS
CN Benzamide, N-[2-(4-fluorophenyl)-4-[3-(1-oxido-4-thiomorpholinyl)-1-azetidinyl]butyl]-N-methyl-3,5-bis(trifluoromethyl)-, monoacetate (9CI) (CA INDEX NAME)

CM 1

CRN 810679-72-2
CMF C27 H30 F7 N3 O2 S

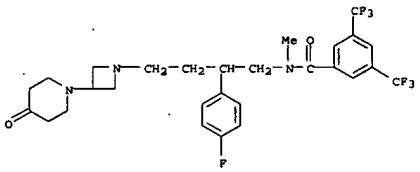
L4 ANSWER 10 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



CM 2

CRN 64-19-7
CMF C2 H4 O2

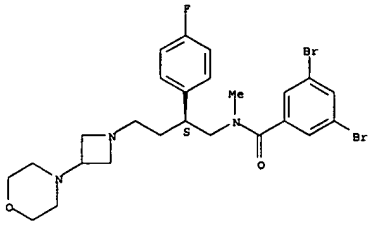
RN 810679-76-6 CAPLUS
CN Benzamide, N-[2-(4-fluorophenyl)-4-[3-(4-oxo-1-piperidinyl)-1-azetidinyl]butyl]-N-methyl-3,5-bis(trifluoromethyl)- (CA INDEX NAME)



RN 810679-97-1 CAPLUS
CN Benzamide, 3,5-dibromo-N-[(2S)-2-(4-fluorophenyl)-4-[3-(4-morpholinyl)-1-azetidinyl]butyl]-N-methyl- (CA INDEX NAME)

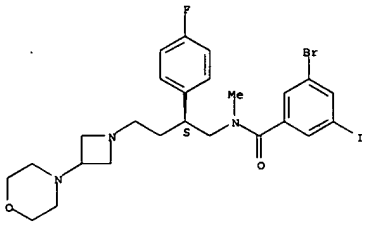
Absolute stereochemistry.

L4 ANSWER 10 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



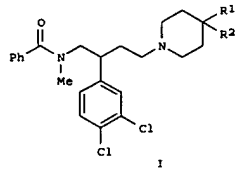
RN 810680-24-1 CAPLUS
CN Benzamide, 3-bromo-N-[(2S)-2-(4-fluorophenyl)-4-[3-(4-morpholinyl)-1-azetidinyl]butyl]-5-iodo-N-methyl- (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 11 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2003:442765 CAPLUS
DOCUMENT NUMBER: 139:245960
TITLE: 4-Amino-2-(aryl)-butylbenzamides and Their conformationally constrained analogues. Potent antagonists of the human neurokinin-2 (NK2) receptor
AUTHOR(S): MacKenzie, A. Roderick; Marchington, Allan P.; Middleton, Donald S.; Newman, Sandra D.; Selway, Christopher N.; Terrett, Nicholas K.
CORPORATE SOURCE: Department of Discovery Chemistry, Pfizer Global Research and Development, Sandwich, Kent, CT13 9NJ, UK
SOURCE: Bioorganic & Medicinal Chemistry Letters (2003), 13(13), 2211-2215
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 139:245960
GI



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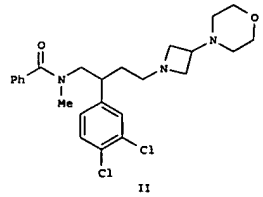
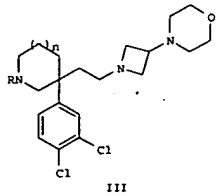


II



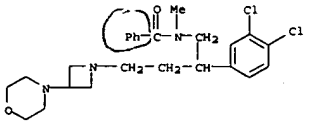
III

AB A library, evaluating a range of piperazines, piperidines and acyclic amines, as replacements for the 4-hydroxy-4-phenylpiperidine moiety in lead I (R1 = Ph, R2 = OH) was prepared These efforts identified the 4-(1-benzimidazolone)piperidine analog I (R1 = 1-benzimidazolonyl, R2 = H)
which was further optimized using classical single-compound synthesis to yield the 3-(4-morpholino)azetidine II. Conformationally constrained

L4 ANSWER 11 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

analogs of II, III (R = PhCO, n = 0; R = PhCO, 4-MeOC6H4, PhSO2, etc., n = 1), generally offered no potency advantage in this particular series.

IT 596105-92-9P
RL: BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of 4-amino-2-(aryl)-butylbenzamide analogs, their human neurokinin-2 (NK2) receptor binding, rabbit pulmonary artery functional
activity, and structure-activity relationship)
RN 596105-92-9 CAPLUS
CN Benzamide, N-[2-(3,4-dichlorophenyl)-4-[3-(4-morpholinyl)-1-azetidinyl]butyl]-N-methyl- (CA INDEX NAME)



REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT